April 8, 2002
James A. Deyo D.V.M., Ph.D., D.A.B.T.
Eastman Chemical Company
P.O. Box 431
Kingsport, TN 37662

Dear Dr. Deyo:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 3-Ethoxypropionic Acid Ethyl Ester, posted on the ChemRTK HPV Challenge Program Web site on November 14, 2001. I commend the Eastman Chemical Company and the Dow Chemical Company for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Eastman Chemical Company and the Dow Chemical Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-s-

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
3-Ethoxypropionic Acid Ethyl Ester

The sponsors, Eastman Chemical Company and the Dow Chemical Company, submitted a test plan and robust summaries to EPA, dated October 4, 2001, for 3-ethoxypropionic acid ethyl ester (CAS No. 763-69-9). EPA posted the submission on the ChemRTK HPV Challenge Web site on November 14, 2001.

SUMMARY OF EPA COMMENTS

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Data. The submitters need to provide measured vapor pressure and water solubility data.

2. Environmental Fate Data. The submitters need to provide measured stability in water data.

3. Health Endpoints. EPA agrees that data are adequate for the purposes of the HPV Challenge Program. However, the submitters need to address a number of deficiencies in the robust summaries.

4. Ecotoxicity. EPA agrees that the aquatic studies for fish and daphnia are adequate for the purposes of the HPV Challenge Program. However, EPA reserves judgment on the algal data and requests a copy of the full report to evaluate the adequacy of the available data.

EPA requests that the Submitters advise the Agency within 60 days of any modifications to this submission.

EPA COMMENTS ON THE 3-ETHOXYPROPIONIC ACID ETHYL ESTER CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

EPA agrees that the submitters' approach to these endpoints, except for vapor pressure and water solubility, is acceptable for the purposes of the HPV Challenge Program. The submitters need to provide measured values for vapor pressure and water solubility. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Environmental Fate (Photodegradation, Stability in Water, Biodegradation, Fugacity).

EPA agrees that the submitters' approach to these endpoints, except for stability in water, is acceptable for the purposes of the HPV Challenge Program.

Stability in Water.

The submitters state that 3-ethoxypropionic acid ethyl ester is not readily hydrolyzed, with estimated half-lives of 102.8 days and 2.8 years at pH values of 8 and 7, respectively, using the HYDROWIN v. 1.67

estimation model. EPA prefers that the submitters provide measured data for stability in water. Having accurate measured water stability data is important because it provides information on the persistence of a chemical in the aquatic environment. Furthermore, according to OECD Guideline 111, a compound that has a half-life of greater than one year at 25EC is considered hydrolytically stable and further testing is not required. As the half-life of this compound at pH 8 is less than one year, the submitters need to provide measured hydrolysis data.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

EPA agrees that data are adequate for purposes of the HPV Challenge Program. However, the robust summary for developmental toxicity needs to be modified. (See "Specific Comments on Robust Summaries" below.)

Ecotoxicity (fish, invertebrate and algal toxicity).

EPA agrees that data are adequate for fish and daphnia for purposes of the HPV Challenge Program. However, EPA questions the validity of the algal data. It was reported in the robust summary that there was no effect on algal growth at a single concentration in a limit test. However, the effective concentration for growth inhibition is predicted to be significantly lower than the concentration tested, based on structure-activity relationships (ECOSAR). Also, the basis for selecting the test concentration was not reported. EPA requests a copy of the full report from this study to determine if additional testing is needed for this endpoint.

Specific Comments on the Robust Summaries

Health Effects

Acute Oral Toxicity. For the cited supplementary study, the submitters need to add the date, report title, and report number.

Acute, Repeated Dose, and Reproductive Toxicity (Inhalation). The submitters need to indicate the method by which the test atmosphere was generated (e.g., as aerosol, vapor, etc.).

Genetic Toxicity - Chromosomal Aberration. The submitters need to add the study title, the concentration levels, the number of replicates/concentration, and the number of metaphases per concentration that were examined.

Developmental Toxicity (Inhalation). For both the rat and rabbit studies, the submitters need to state the method by which the test atmosphere was generated (e.g., aerosol, vapor, etc.). For the rat study, EPA disagrees with the selection of the NOAEL of 1000 ppm for developmental toxicity because increased incidences of soft tissue alterations and skeletal variations were seen in litters at this dose level with slightly greater than minimal maternal toxicity.

Follow-up Activity

EPA requests that the Submitters advise the Agency within 60 days of any modifications to this submission.